S/N NEW FILING

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	MERCKEN ET AL.	Examiner:	UNKNOWN
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Filed:	HEREWITH	Docket No.:	12546.4USC1
Title:	MONOCLONAL ANTIBODIES DIRECTED AGAINST THE MICROTUBULE-ASSOCIATED PROTEIN TAU		

CERTIFICATE UNDER 37 CFR 1.10
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By: Chata Lambert
Name: CHATA LAMBERT

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Before taking up the present continuation application for examination, please amend the claims as follows:

In the Claims

Please cancel claims 1 and 2 without prejudice.

Please add claims 20-29 as follows:

20. (New) A monoclonal antibody which forms an immunological complex with a phosphorylated epitope present in a human abnormally phosphorylated tau protein, wherein said tau protein is obtained from a brain homogenate, isolated from the cerebral cortex of a patient having Alzheimer's disease or having died of Alzheimer's disease.

21. (New) The monoclonal antibody according to claim 20 wherein said monoclonal antibody forms an immunological complex

(a) with a peptide YSSPG*S*PGT (SEQ ID NO 1) or YSSPG*S*PGT (SEQ ID NO 2), wherein said peptide is phosphorylated at a position marked with *,

(b) or with any other peptide forming an immunological complex with a monoclonal antibody, which forms a complex with peptide YSSPG*S*PGT (SEQ ID NO 1) or YSSPG*S*PGT (SEQ ID NO 2).

22. (New) The monoclonal antibody according to claim 20 selected to exclude forming an immunological complex with:

(a) normal tau protein;

(b) tau protein present in brain homogenates derived from human brain, the homogenates being isolated from a patient having died of a non-neurological disorder;

(c) a phosphorylated epitope treated with a dephosphorylating agent; and

(d) any variant peptide treated with a dephosphorylated agent.

23. (New) The monoclonal antibody according to claim 20, wherein said monoclonal antibody:

(a) forms an immunological complex with the abnormally phosphorylated forms of tau protein, present in homogenates of human brain of a patient having died of Alzheimer's disease; and wherein

(b) abnormally phosphorylated tau proteins present an apparent molecular weight which is higher than that of normal tau proteins, obtained from brain homogenates isolated from a patient having died of non-neurological disorders; and wherein

(c) the apparent molecular weight can be decreased to that of normal tau proteins upon treatment of said abnormally phosphorylated tau proteins with a dephosphorylating agent.

24. (New) A hybridoma, which secretes a monoclonal antibody according to claim 20.

25. (New) A process for isolating a hybridoma secreting a monoclonal antibody according to claim 20 comprising the steps of:

(a) immunizing the spleen cells of an animal with an antigen recognized by the monoclonal antibody deposited at ECACC on October 8 under No. 91100806;

(b) fusing said immunized cells with myeloma cells under hybridoma-forming conditions; and

(c) selecting those of the hybridomas which secrete said monoclonal antibody.

26. (New) A process for producing monoclonal antibodies according to claim 20 comprising the steps of:

(a) culturing the selected hybridomas according to claim 24, in an appropriate medium culture;

(b) recovering the monoclonal antibodies excreted by said selected hybridomas; or alternatively; and

(c) implanting the selected hybridomas of claim 24 into the peritoneum of a mouse and, when ascites has been produced by the animal, recovering the monoclonal antibodies then formed from said ascites.

27. (New) Process for the detection or diagnosis in vitro of brain disease involving PHF and abnormally phosphorylated tau protein, comprising the steps of:

(a) contacting a monoclonal antibody according to claim 20, with a preparation of NFT or a detergent-extracted brain homogenate isolated from a patient having had Alzheimer's disease under conditions suitable for producing an antigen-antibody complex; and

(b) separating the antigen from said complex and detecting the antigen sought in a purified form wherein the presence of the antigen in quantities higher than control indicates said brain disease involved PHF abnormally phosphorylated tau protein.

28. (New) A process for the detection or diagnosis in vitro of brain disease involving PHF and abnormally phosphorylated tau protein, comprising the steps of:

(a) bringing a sample of brain homogenate, or of cerebrospinal fluid, or of serum from a patient suspected of suffering from a neurological disorder involving abnormally phosphorylated tau protein and PHF into contact with a monoclonal antibody according to claim 20, under conditions suitable for producing an antigen-antibody complex; and

(b) detecting the immunological binding of said antibody to said sample of brain homogenate, or cerebrospinal fluid, or serum.

29. (New) A kit for the in vitro diagnosis of one of the following diseases: Alzheimer's disease, Down's syndrome, Pick's disease, SSPE and other neurological disorders in which abnormally phosphorylated tau protein or paired helical filaments are implicated, the kit comprising:

(a) a first monoclonal antibody according to claim 20 deposited on a microplate;

(b) a second antibody recognizing a different epitope from said first monoclonal antibody which is a monoclonal antibody recognizing an epitope of normal tau, or of abnormally phosphorylated tau protein or which is a polyclonal antibody of normal tau, or of abnormally phosphorylated tau; and

(c) a marker for specific tagging or coupling with said second antibody; appropriate buffer solutions for carrying out the immunological reaction between said first monoclonal antibody and a test sample and the second antibody and the marker.

REMARKS

These new claims are generally patterned after the claims allowed in the parent case and are supported in the specification. No new matter has been added. Thus, it is believed that these claims are in condition for allowance. Notification to effect is earnestly solicited.

If the Examiner believes that a telephone conference will expedite prosecution of this application, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below.

Respectfully submitted,

MERCHANT & GOULD P.C.
P.O. Box 2903
Minneapolis, Minnesota 55402-0903
(612) 332-5300

Date: Dec 11, 2000

Mark T. Skoog
Reg. No. 40,178
MTS:MAD

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PATENT TRADEMARK OFFICE